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Are Anti depressants Effective in the Treatment of Depressed Patients Who Do Not Seek Psychotherapy?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

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Abstract

OBJECTIVE: The objective of this selective EBM review is to determine whether or not anti depressants are effective in the treatment of depressed patients who do not seek psychotherapy.

STUDY DESIGN: Review of all English language primary randomized controlled trials published from 2000-2009.

DATA SOURCES: Three randomized controlled trials were found using OVID, Medline, EbscoHost, Pubmed, and Cochrane databases.

OUTCOMES MEASURED: The three trials measured the change in the severity of depression symptoms using different outcomes: The Montgomery Asburg Depression Scale, Hamilton Depression Rating Scale, and Hopkins Symptom Checklist Depression Scale.

RESULTS: Hermens et al. found that the use of usual care and paroxetine is no more effective than usual care at fifty-two weeks. Barrett et al. found that paroxetine is no more effective than placebo in the treatment of depression at eleven weeks. Williams et al. found that paroxetine is more effective than placebo in decreasing depressive symptoms, in older adults, at eleven weeks.

CONCLUSIONS: The work of Hermens and Barrett demonstrated that paroxetine is no more effective than usual care in the treatment of depression within the general population. Williams RCT's demonstrates that paroxetine may be effective in the treatment of depression in older adults.

KEY WORDS: depression, anti depressants, treatment + depression

INTRODUCTION

Depression is a serious mental illness characterized by a depressed mood in conjunction with fatigue, changes in sleep patterns, changes in eating patterns, irritability, and the inability to enjoy things that one previously enjoyed. Because depression is a spectrum disorder that ranges from dysthymia to major depression, the treatments are numerous and diverse. It can include psychotherapy, medication, electroconvulsive therapy, or any combination. The first line treatment for people with depression involves antidepressant therapy, most commonly in the form of selective serotonin reuptake inhibitors (SSRI's), together with outpatient psychotherapy[4]. It is not currently known whether antidepressant therapy is effective without concurrent psychotherapy. This paper analyzes three randomized controlled studies to determine the effectiveness of antidepressants when not in conjunction with psychotherapy.

Despite great progress in the treatment and diagnosis of depression, it still continues to be incredibly common within the general population. The lifetime prevalence of major depression is 7-12% and 20-25% in men and women respectively [2], which in recent years has accounted for up to 9.7 million office visits[5]. Among patients with health related comorbidities the prevalence is believed to be as high as 20-40%[5]. The yearly cost of depression in the United States is projected to be as high as twenty six billion dollars; with indirect costs as high as fifty billion dollars[5].

Due to time constraints, managed care, and the stigma attached with psychotherapy, physician assistants will find themselves with patients for whom psychotherapy is not an option. Keeping in mind the prevalence, costs, morbidity, and

mortality associated with depression, the need for determining the effectiveness of antidepressants as a sole treatment becomes apparent.

OBJECTIVE

The objective of this selective EBM review is to determine whether or not antidepressants are effective in the treatment of depressed patients who do not seek psychotherapy.

METHODS

In order for studies to be included for review, all patients had to be over the age of 18, in the outpatient setting and also have a clinical diagnosis of depression using the Diagnostic and Statistic Manual of Mental Disorders (DSM). The intervention for all studies was oral Paroxetine and the comparison group was no treatment other than usual care or a placebo pill. The outcomes that were measured in each study attempted to capture the change in depressive symptoms. The three studied included are Randomized Controlled Trials (RCT's).

Peer reviewed journals written in the English language were searched using OVID, Medline, EbscoHost, Pubmed, and Cochrane databases between December 2010 and January of 2011. The key words used in searches were depression, antidepressants, and treatment+ depression. The inclusion criteria for each study required that it be an RCT with Patient Oriented Evidence that Matters (POEM) and have been completed in the past 10 years. The exclusion criteria were studies with patients under 18, patients currently on antidepressants, and those having previous issues with substance abuse. All searches were conducted by the author and Stephanie Ferretti of the Philadelphia College

of Osteopathic Medicine Library. All studies were published. The statistics reported include p value, relative risk ratio (RRR), and numbers needed to treat (NNT).

A. Table 1 - Demographics & Characteristics of included studies

Study	Type	# patients	Age (yrs)	Inclusion Criteria	W/D	Interventions
Barrett, 2001 (1)	RCT	241	18-59	3/9 DSM-III-R symptoms for major depression for at least 4 weeks, DSM-III-R criteria for dysthymia or minor depression, >10 on HDRS	20	Paroxetine
Hermens, 2007 (3)	RCT	181	18+	3-6/9 DSM-IV symptoms of depression, significant distress/impairment, symptoms daily for 2 weeks	21	Paroxetine
Williams, 2000 (5)	RCT	415	60+	Minor depression/dysthymia diagnosed by DSM-IIIR, HDRS >9, 3-4 symptoms for at least 4 weeks	65	Paroxetine

OUTCOMES MEASURED:

The study performed by Hermens et al. took place in the Netherlands with patients recruited by primary care physicians. Upon identification of possible patients, research assistants conducted baseline interviews in which the patient received an explanation of the study and then informed consent was obtained. The patients were then randomized into usual care plus antidepressants or usual care alone. At the conclusion of the study the patient's depressive symptoms, as measured by The Montgomery Asberg Depression Rating Scale, were compared to their symptoms at intake.

The study performed by Barrett et al. took place in New Hampshire and Washington with patients recruited by primary care physicians at these two sites. Patients who met all criteria were consented and randomized to paroxetine, placebo, or Problem-Solving Treatment for Primary Care. At the conclusion of the study the patients' depressive symptoms, as measured by the Hamilton Depression Rating Scale, were compared to their symptoms at intake.

The study performed by Williams et al. took place at four geographically and clinically diverse sites (location unspecified) with patients recruited through referral from various primary care clinics. Patients who met all criteria were consented and randomized to placebo, paroxetine, or Problem-Solving Treatment for Primary Care. At the conclusion of the study the patients' depressive symptoms were measured using the 20-item Hopkins Symptom Checklist Depression Scale.

RESULTS:

The study by Hermens et al. from 2007 used patients over the age of 18 with a diagnosis of minor or mild-major depression. The test group was given 20 mg/day of oral paroxetine and usual care for three months. The control group received only usual care for three months. Patients in the test group could increase their dose of paroxetine to 40mg a day, if at 4 weeks their clinical response was poor. The study was conducted for a total of 52 weeks. Hermens et al. reported that greater than 25% of patients were not treated according to protocol. Table 2 shows that there was a 14.7 point decrease in the Montgomery Asberg Depression Rating Scale score from baseline at 52 weeks with usual care and paroxetine. For patients with usual care only, there was a decrease of 12.6

points. The CI at 95% is wide at -6.2;1.9 with a standard deviation of 24.2 The data presented is continuous and cannot be converted to dichotomous data because the author does not include individual scores for the patients, only the average of all test subjects. This study fails to show that usual care and paroxetine are any more effective than usual care at 52 weeks.

Table 3: The Effect of Antidepressants on Montgomery Asberg Depression Rating Scales

Hermens et al.				
Outcomes measured	Usual Care + Paroxetine	Usual Care	Mean difference	Confidence interval at 95%
Change in MADRS* from baseline	-14.8	-12.7	2.1	-6.2; 1.9

*Montgomery Asberg Depression Rating Scales

The study by Barrett et al. from 2001 used patients aged 18-59 with minor depression or dysthymia. The test group received oral paroxetine that was started at 10mg/day and increased to 20mg/day at week 2. At week 4 or 6 the dose could be further increased to 30mg per day and at week 6 or 8 to 40mg if there was limited clinical improvement. The control group received a placebo that was titrated in the same fashion. As is shown in table 4, 60.7% of those who received paroxetine and 65.6% of those who received placebo, achieved remission as defined by a score of 6 or less on the Hamilton Depression Rating Scale (p= .906). The relative benefit increase was found to be -0.0747, absolute benefit increase -4.90, and number needed to treat= -20.0. This study fails to show that paroxetine is any more effective than placebo in the treatment of depression at 11 weeks.

Table 4: The Effect of Antidepressants on Rate of Remission as Defined by Hamilton Depression Rating Scale

Barrett et al.						
Outcomes measured	Paroxetine	Placebo	*p*	RBI	ABI	NNT
Remission Rate (%)	60.7	65.6	-0.906	-0.0747	-4.90	-20.0

The study by Williams et al. from 2000 used patients with a clinical diagnosis of dysthymia and minor depression over the age of 60. Oral paroxetine was administered to their test group which was started at 10mg/day and then subsequently increased to 20mg/day at week 2. At week 4 or 6 the dose could be further increased to 30mg per day and at week 6 or 8 to 40mg if clinical improvement was limited. The control group received placebo that was titrated in an identical fashion. As is shown in table 5, 53.1% of those who received paroxetine and 49.1% of those who received placebo achieved remission as defined by a score of 6 or less on the Hamilton Depression Rating Scale (p= 0.004). The relative benefit increase was found to be 0.0815, absolute benefit increase 4, and number needed to treat= 25. This study shows that paroxetine is more effective than placebo in the treatment of depression at 11 weeks.

Table 5: The Effect of Antidepressants on Rate of Remission as Defined by the Hopkins Symptom Checklist Depression Scale

Williams et al.						
Outcomes measured	Paroxetine	Placebo	*p*	RBI	ABI	NNT
Remission Rate (%)	53.1	49.1	-0.906	-0.0815	4	25

In the study by Williams at al. 9.7% of patients taking paroxetine dropped out due to adverse side effects whereas 5.7% of those taking placebo dropped out due to side effects. NNH was calculated to be 27. This is the only study, of the three, to give data on the patients who dropped out as a result of adverse side effects. None of the studies give any indication as to the side effects or adverse reactions patients experienced.

Table 5: Harms Associated With Treatment

Study	RRI	ARI	NNH
Barrett, 2001 (1)			
Hermens, 2007 (3)			
Williams, 2000 (5)	.64	3.4	27

DISCUSSION:

There was a great degree of incongruence between the three studies included for review. The most important being that the only study to show paroxetine as an effective treatment only included patients over the age of sixty. This leaves questions as to whether paroxetine is an effective treatment in this specific population. Other discrepancies

between the studies include differences in the length of treatment as well as differences in disease severity of participants.

Although the efficacy of selective serotonin reuptake inhibitors (SSRIs) as treatment for depression is questionable, they have long been used as part of the treatment in numerous other conditions including panic disorder, obsessive compulsive disorder, social phobia, post traumatic stress disorder, and premenstrual dysmorphic disorder. None of the included studies disclosed the cause of patient drop out as a result of adverse side effects, but it is apparent that SSRIs are not without side effects. Current black box labeling of SSRIs warn of an increased risk of suicide in patients with major depressive disorders, during the first two months of treatment. In addition, patients taking SSRIs are at risk for serotonin syndrome, which is a life threatening disorder characterized by excess serotonin that manifests itself as restlessness, hallucinations, loss of coordination, fast heart beat, rapid changes in blood pressure, increased body temperature, overactive reflexes, nausea, vomiting, and diarrhea. Some of the more minor and yet more common side effects include anxiety, constipation, insomnia, erectile dysfunction, and decreased libido[4].

CONCLUSION:

Using the three studies included for systematic review, it cannot be concluded that antidepressants, as monotherapy, are an effective treatment for depression in the general population. However, based on the results of the study by Williams et al, antidepressants may be effective in adults over the age of 60 with a diagnosis of depression.

Given the profound economic and social impact of depression, it would be beneficial to further study the efficacy of antidepressants as monotherapy in specific subpopulations including teens and middle-aged adults. It would also be advantageous to closely study their effect on the specific clinical presentations of depression, namely dysthymia, mild depression, and major depression. Lastly, it would be helpful to know the effectiveness of antidepressants at distinct time intervals within a depressive episode.

REFERENCES

1. Barrett JE, Williams Jr. JW, Oxman TE, et al. Treatment of Dysthymia and Minor depression in Primary Care. *J Fam Pract.* 2001;50(5):405-412.

2. Cole SA, Christensen JF, Raju Cole M, Cohen H, Feldman MD. Chapter 22. Depression. In: Feldman MD, Christensen JF, eds. Behavioral Medicine: A Guide for Clinical Practice. 3rd ed. New York: McGraw-Hill; 2011. http://www.accessmedicine.com/content.aspx?aID=6441215. Accessed October 1, 2011.

3. Hermens ML, van Hout HP, Terluin B, et al. Clinical effectiveness of usual care with or without antidepressant medication for primary care patients with minor or mild-major depression: a randomized controlled equivalence trial. BMC Med. 2007;5:36.

4. O'Donnell JM, Shelton RC. Chapter 15. Drug Therapy of Depression and Anxiety Disorders. In: Brunton LL, Chabner BA, Knollmann BC, eds. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 12nd ed. New York: McGraw-Hill; 2011. http://www.accessmedicine.com/content.aspx?aID=16663059. Accessed December 14, 2011.

5. Wade A, Häring J. A review of the costs associated with depression and treatment noncompliance: The potential benefits of online support. International Clinical Psychopharmacology [serial online]. September 2010;25(5):288-296. Available from: PsycINFO, Ipswich, MA. Accessed October 1, 2011.

6.William JW, Jr, Barrett J, Oxman T, et al. Treatment of dysthymia and minor depression in primary care: A randomized controlled trial in older adults. JAMA. 2000;284(12):1519-1526.